UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/783,487 | 02/14/2001 | Tito Andrew Serafini | 10239-010 | 7095 |

20583 7590 04/14/2004

JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

| EXAMINER | |
|---|---|
| WOITACH, JOSEPH T | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1632 | |

DATE MAILED: 04/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Advisory Action | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/783,487 | SERAFINI, TITO ANDREW | |
| | Examiner | Art Unit | |
| | Joseph T. Woitach | 1632 | |

*--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

THE REPLY FILED 24 March 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *24 March 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☒ The proposed amendment(s) will not be entered because:

(a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: *See Continuation Sheet*.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☐ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1-27 and 32-60*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)( PTO-1449) Paper No(s). _____.

10.☐ Other: _____

Joe Woitach
AU1632

Continuation of 2. NOTE:

The proposed amendment to claim 1 of specific expression characteristics of the first sequence encompass embodiments that previously were not searched nor specifically considered. Further, it raises issues under 35 USC 112, second paragraph, because it is no clear how one can provide a regulatory sequence for expression, however the same sequence was not used in expression. Moreover, as evidenced in the art, even suppling an endogenous gene on a BAC provides an expression pattern that is not the same as seen for the endogenous gene. It is unclear if the claim encompasses the expression of a gene in a tissue that in which it is not normallly expressed, or if the proposed amendment attepts to exclude sequences where the promoter and expressed sequence are part of the same gene. Finally, if the amendment attempts to exclude the insertion of complete gene sequences, it would alter the scope of the claim requiring a new search of the relevant art and futrther consideration under 35 USC 112, 1st and second paragraphs, and 35 USC102/103.

Continuation of 5. does NOT place the application in condition for allowance because:

It is noted that the amendment has not been entered. However to the extent that Applicants' arguments apply to the instant claims arguments are not found persuasive. Applicants argue that the invention is fully enabled and that the artisan can provide larger pieces o a promoter for example in the context of a BAC vector, noting specific results in newly supplied references (see attached Appendix). This is not found persuasive because review of the teachings of supplied references support the basis of the rejection. While the size of the promoter may matter to some extent in particular casess, Giraldo et al. teaches that copy number (page 86) also matters With the use of a YAC, there is an inherent problem with stability and thus the presence in stable lines (page 91). The results of Cavelier et al demonstrate that expression from a BAC clones can vary and is different in tissues assayed, some demonstrating higher expression leve and some lower or non-detectable levels (see figure 2). Rui et al. teach that using the same construct expression differend among severa independnet lines (page H1406). The teachings of the references provide further support for the need of more detailed guidance, and no a simple approach that larger sequences will remedy the art recognized limitations for the use of heterologous promoters in transgenes t practice the claimed method. In addition, the teachings further support the basis of the 35 USC 112, second paragraph, rejection in light of the varied expression levels one can obtain even with the same construct in separate independent lines. Examiner acknolwedges that even prior to the filing date of the instant application that many transgenic animals comprising large promoter sequences have been constructed (for example as outlined by Giraldo et al. (see Table 1), however the present specification provides no further guidance than presented in these prior art documents for making the claimed invention. With respect to genes associated with specific disorders, Applciants argue that these are readily known in the art and point ot Pamboz et al. and Schmauss et al. as supporting evidence. Applicants arguments are not found persuasive because again these reference further support the basis of the rejection. In this case, Schmauss et al. teach that dipamine D3 receptor expression is decreased in patients with schizophrenia, however knock-out mice that have no expression of the dopamine D3 receptor are phenotypically normal (page 14476), other genes change expression to compensate for the alteration, and there is not a clear coorelation with schizophrenic behavior in the KO mice and is 'paradoxical' to phenotypes predicted from humans (page 14480). The methodology of generating transgenics is relatively straightforward and simple to the skilled artisan, however the consequence of inserting and exprssing a gene and the resulting phenotype is sitill unpredictable and impirical. The present specification provides an outline to make a product however fails to provide the necessary guidance to overcome art accepted limitations.

With repsect ot the art rejection it is noted again that the claim amendments have not been entered, and Applicants' arguments would not apply to the pending claims. However, it is noted that it appears that Leinwand would still anticipate the proposed claims because the term 'a characterizing gene' is associated with (b) the regulatory sequences (see claim 1), not the gene expressed. In addition, it would meet the limitation wherein the gene was not expressed before the animal was generated.

With respect to the double patenting rejection, Applicants willingness to cancel conflicting claims is noted, however the rejection can not be held in abeyance, and is maintained for the reasons of record.